

Remarks

Claims 1, 3-5, 7, 8, 10, 12, 16-21, 24-34, 37-40, and 42-48 were pending in the subject application. By this Amendment, claims 1, 3-5, 7, 8, 17-21, 25-29, 33, 34, 37, 38, 40, 42, and 44-48 have been canceled, and new claims 49-51 have been added. The undersigned avers that no new matter is introduced by this Amendment. Support for the new claims and amendments can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 10, 12, 16, 24, 30-32, 39, 43, and 49-51 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

By this Amendment, claims 49-51 have been added. Support for claims 49-51 can be found, for example, at page 10, lines 1-5; page 16, lines 1-8; page 17, lines 20-23; and page 21, lines 7-23, of the specification as filed.

Claims 10, 12, 16, 24, 30-32, and 43 are rejected under 35 USC §103(a) as obvious over Boussif *et al.* (European Patent No. 1013772). Applicant respectfully traverses this ground of rejection.

The Examiner asserts that Boussif *et al.* teach methods of gene therapy to respiratory epithelium using nanoparticles comprising a lipopolyplex (particle of a cationic lipid, a cationic polymer, and a nucleic acid) which can include chitosan as the cationic polymer component. The Examiner concludes that it would have been obvious to a person of skill in the art at the time of the invention to use a lipopolyplex composition of chitosan, a lipid, and a polynucleotide for delivery and expression of a polynucleotide to the respiratory epithelium of a mammal. Specifically, at page 7 of the Office Action, the Examiner notes that the graph of Figure 4 shows that polyplexes (particles of nucleic acid and chitosan) induce the most interleukin-6 (IL-6), lipoplexes (particles of nucleic acid and lipid) induce the least IL-6, and lipopolyplexes induce an amount of IL-6 between the other two formulations, and thus concludes that “as the lipopolyplexes comprise a blend of both chitosan and lipid, it is not surprising to find that the amount of IL-6 induced falls between the other two formulations.” Applicant respectfully submits that this is an over-simplification.

While column 6 in the bar graph of Figure 4 of the subject specification does show an IL-6 level that is in between that observed from particles of chitosan and nucleic acid (column 4, Chit+pVAX) and particles of lipid and nucleic acid (column 5, Lipid+pVAX), the amount of IL-6 in column 6 is much lower than that from particles of chitosan and nucleic acid and nearly as low as that from particles of lipid and nucleic acid. When taken in the context of IL-6, a pro-inflammatory cytokine, within the respiratory epithelium, this is a significant and unexpected result. Moreover, one of ordinary skill in the art would not have expected the decrease in IL-6 when an increase in transfection efficiency in lung epithelial cells is observed (Figure 3 of specification). This favorable profile means that the particles represent an efficient delivery system that is less likely to contribute to airway inflammation and damage.

As indicated in the Manual of Patent Examining Procedure (MPEP 716,02(a)), “a greater than expected result is an evidentiary factor pertinent to the legal conclusion of obviousness ... of the claims at issue.” *In re Corkill*, 711 F.2d 1496, 226 USPQ 1005 (Fed. Cir. 1985). Evidence of a greater than expected result may also be shown by demonstrating an effect that is greater than the sum of each of the effects taken separately (*i.e.*, “synergism”). *Merck & Co. Inc. v. Biocrraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989). Evidence of unobvious or unexpected advantageous properties, such as superiority in a property the claimed compound shares with the prior art, can rebut *prima facie* obviousness. “Evidence that a compound is unexpectedly superior in one of a spectrum of common properties . . . can be enough to rebut a *prima facie* case of obviousness.” No set number of examples of superiority is required. *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987).

Applicant respectfully asserts that the claimed invention is not obvious over the cited reference. Accordingly, reconsideration and withdrawal of the rejection under 35 USC §103(a) is respectfully requested

Claim 39 is rejected under 35 USC §103(a) as obvious over Boussif *et al.* (European Patent No. 1013772) as applied to claim 10 above, and further in view of Vijayanathan *et al.* (*Biochemistry*, 2002, 41:14085-14094). In addition, claim 47 is rejected under 35 USC §103(a) as obvious over Boussif *et al.* (European Patent No. 1013772) as applied to claim 10 above, and further in view of

Han *et al.* (*Molecular Therapy*, October 2000, 2(4):302-317). Applicant respectfully traverses these grounds of rejection.

Applicant's aforementioned remarks concerning IL-6 are incorporated herein by reference.

As the Examiner is undoubtedly aware, inherency may not be established by probabilities or possibilities regarding what may have resulted in the prior art. *In re Oelrich*, 212 USPQ 323, 326 (CCPA 1981). "The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *Hansgird v. Kemmer*, 40 USPQ 665, 667 (CCPA 1939). Applicant respectfully submits that the Office Action does not establish that the compositions of Vijayanathan *et al.* are identical or substantially identical, or obtained by an identical or substantially identical process, in accordance with the precepts of *In re Best*, 195 USPQ 430, 433 (C.C.P.A. 1977) and MPEP § 2112.01. Applicant respectfully submits that when an Examiner relies upon a theory of inherency, "the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex Parte Levy*, 17 USPQ2d 1461, 1464 (BPAI 1990). Here, the Examiner asserts that "since the teachings of Vijayanathan *et al.* encompass nanoparticles comprising the same materials as Boussif *et al.* and the instant claims, the examiner concludes the arrangement of such nanoparticles into a hexagonal lattice is a natural consequence of the chemical nature of these particles." Applicant respectfully submits that even if the compositions of Vijayanathan *et al.* share some ingredients with particles recited in the claims under examination, this is insufficient to support the conclusion that they are the same and, therefore, have the same properties and characteristics.

Initially, it is the Examiner's burden of providing factual evidence and/or technical reasoning to support the determination of inherency. See *In re Spada*, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990); *In re King*, 231 USPQ 131, 138-139 (Fed. Cir. 1986). Applicant respectfully submits that the Examiner has not met this burden. The presence of inherent matter must be grounded on more than speculation, it must be a certainty. *Ethyl Molded Product Co. v. Betts Package Inc.*, 9 USPQ 2d 1001, 1032-1033 (I.D.KY 1988) ("the doctrine of inherency is available only when the prior inherent event can be established as a certainty. That an event may result from a given set of circumstances is not sufficient to establish anticipation" (emphasis added)). Furthermore, when the reference is silent

about the asserted inherent characteristic, while such a gap in the reference may be filled with recourse to extrinsic evidence, the extrinsic evidence

must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill in the art. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. *In re Robertson*, 49 USPQ 2d 1949, 1950-1951 (Fed. Cir. 1999).

There is no clear and unambiguous disclosure in Vijayanathan *et al.* of the nanoparticle structure recited in claim 39, nor does the Office Action make clear that this is an inevitable result.

Claim 47 has been canceled, rendering the rejection based on Boussif *et al.* in view of Han *et al.* moot.

Applicant respectfully asserts that the claimed invention is not obvious over the cited references. Applicant further asserts that the cited references do not teach or suggest the claimed invention. Accordingly, reconsideration and withdrawal of the rejections under 35 USC §103(a) is respectfully requested.

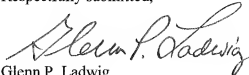
It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicant's agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicant believes that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

Applicant invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



Glenn P. Ladwig
Patent Attorney
Registration No. 46,853
Phone No.: 352-375-8100
Fax No.: 352-372-5800
Address: P.O. Box 142950
Gainesville, FL 32614-2950

GPL/jnw